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TCE Update

Former NAS Moffett Field Restoration Advisory Board Meeting

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TCE Update

- Significance of TCE at Superfund sites
- EPA drinking water standard for TCE is 5 ppb
- No similar EPA standard for vapor intrusion pathway and indoor air
- EPA issued new TCE toxicity on 28 September 2011
- Integrated Risk Information System (IRIS) process
- Projected Regional Screening Levels
- Questions

Integrated Risk Information System - IRIS

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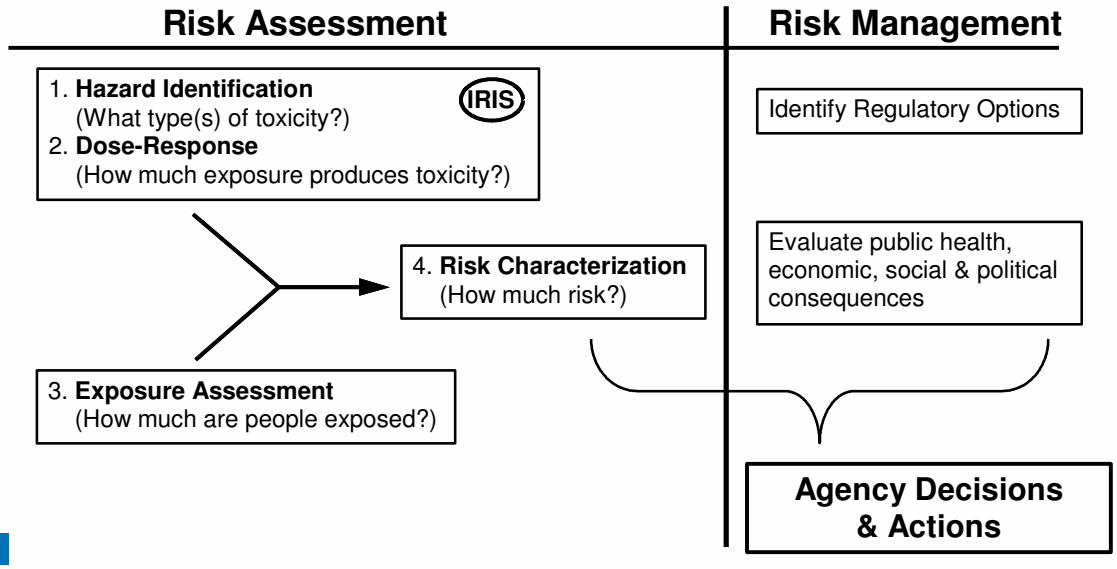
Why is IRIS Important?

Risk Assessment and Risk-Based Cleanup Levels (PRGs) now called Regional Screening Tables (RSLs)



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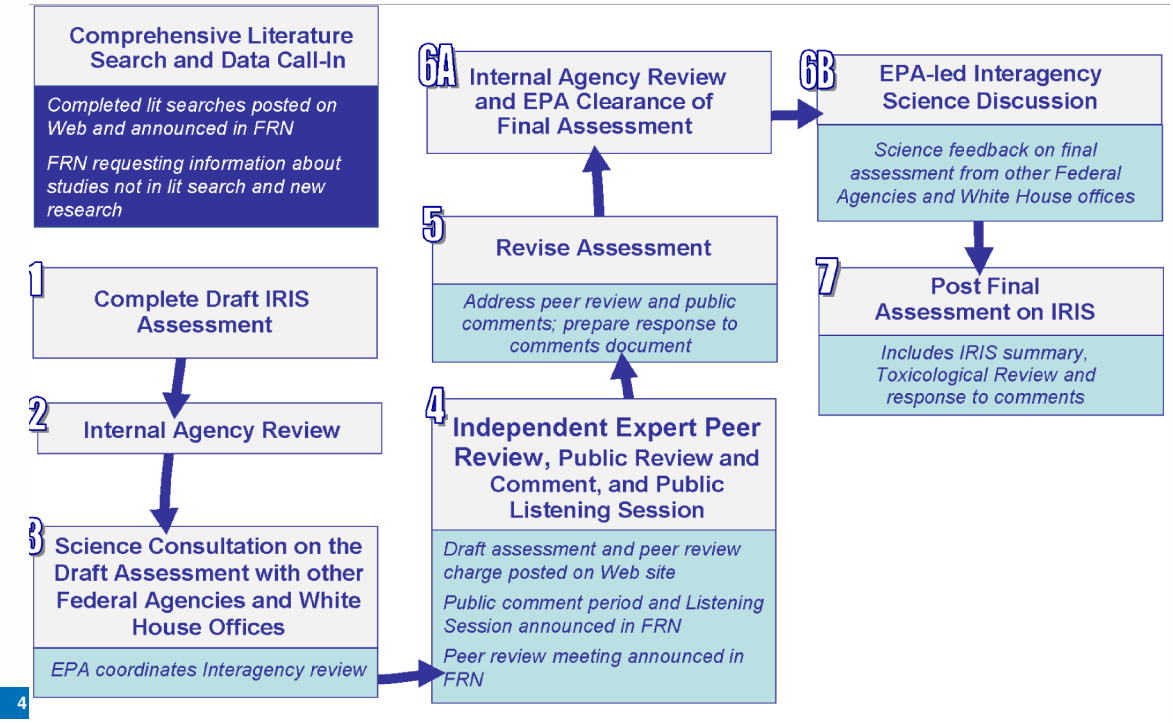
What is Involved in an IRIS Assessment?

- **Review scientific literature for toxicity data**
  - identify useful (scientifically valid) studies
- **Analyze the relevant data**
  - identify critical studies, toxicities
  - quantitative modeling of dose-response
- **Write a toxicological review**
- **Calculate toxicity values for risk assessment**
  - cancer potency factors
  - non-cancer reference doses
- **Publish on IRIS database**

Current IRIS Development Process



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Hazard Assessment

Health Effects associated with TCE

- **Non-cancer**
  - Acute effects-neurological
  - Various organ systems
    - Liver
    - Kidney
  - Immunological
  - Reproductive
  - Developmental
- **Cancer**
  - Kidney
  - Liver
  - Lymphoma
- **Mode of Action**
  - Mutagenic (kidney only)
  - through metabolites

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What's New in the TCE Toxicological Review

- Cancer and Non-cancer values
- Values for both oral and inhalation
- Account for multiple sites of cancer
- Mutagenic mode of action for kidney cancer

Key features of the Final TCE Assessment

- **Main components of External Review Draft retained**
  - Comprehensive review of studies of TCE and TCE metabolites
  - Toxicity review organized by tissue/system
  - Multiple lines of evidence supporting major conclusions of hazard characterization and dose-response assessment
    - Human epidemiologic data
    - Animal toxicity data
    - Mechanistic data
    - State-of-the-art quantitative analyses
- **Implemented virtually all SAB recommendations, resulting in:**
  - **Small (<3-fold) changes in non-cancer RfD and RfC**
  - **No change to carcinogenic classification**
  - **No change to cancer inhalation unit risk or oral slope factor**
  - **No change to application of ADAFs**

Final Dose Response Assessment: Summary

- **Final Non-cancer reference values**
  - RfC and RfD selected are protective of the most sensitive effects, supported by multiple studies/endpoints
  - Most sensitive target organs/systems: adult immunological system, developing fetal heart, developing immunological system
  - Supported by kidney effects

- **Final Cancer risk values**
  - Target sites: kidney cancer, NHL, and liver cancer
  - Apply ADAF to kidney cancer risk only

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Possible TCE screening values

		Current RSL		New RSL		MEW decisions
	endpoint	cancer 10-6	non-cancer	cancer 10-6	non-cancer	
Residential	water ug/L	2	21	~1	3	5 MCL
	air ug/m3	1	10	~0.5	2	1
Industrial	air ug/m3	6	44	~4	9	5

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TCE Update: Take Home

- All EPA programs are looking at the new toxicity values and making the management decisions on how to implement any changes
- In Superfund, EPA has Five-Year Review process and will assess impact of any changes that revised TCE toxicity values have on health-based screening values and risk management decisions at each site

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Questions?

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Where to go for more information on TCE:
http://www.epa.gov/IRIS/ and click on TCE link

Critical effects for the RfC

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- Most sensitive candidate critical effects by domain
- Multiple candidate RfCs in range 0.0003-0.0006 ppm
- Kidney effects considered supporting, not primary.
- **RfC of 0.0004 ppm (2 µg/m^3) based on multiple principal studies/ effects**

EFFECT DOMAIN **Most sensitive candidate critical effects (study)**	**p-cRfC ppm (UF_{comp})**
NEUROLOGIC	
Demyelination in hippocampus (rat/Isaacson et al. 1990)	0.0071 (1000)
KIDNEY	
Toxic nephropathy (rat/NTP 1988)	0.00056 (10)
Toxic nephrosis (mouse/NCI 1976)	0.0017 (300)
↑ kidney weight (rat/Woolhiser et al. 2006)	0.0013 (10)
LIVER	
↑ liver weight (mouse/Kjellstrand et al. 1983b)	1.0 (10)
IMMUNOLOGIC	
↓ thymus weight (mouse/Keil et al. 2009)	0.00033 (100)
↑ anti-dsDNA & anti-ssDNA Abs (mouse/Keil et al. 2009)	0.0033 (10)
REPRODUCTIVE	
↓ ability of sperm to fertilize (rat/DuTeaux et al. 2004)	0.0093 (1000)
DEVELOPMENTAL	
Heart malformations (rat/Johnson et al. 2003)	0.00037 (10)

Critical effects for the RfD

- Most sensitive candidate critical effects by domain
- Multiple candidate RfDs in range 0.0003-0.0005 mg/kg/d
- Kidney effects considered supporting, not primary.
- **RfD of 0.0005 mg/kg/d based on multiple principal studies/ effects**

EFFECT DOMAIN Most sensitive candidate critical effects (study)	p-cRfD or cRfD mg/kg/d (UF_{comp})
NEUROLOGIC	
Demyelination in hippocampus (rat/Isaacson et al. 1990)	0.0092 (1000)
KIDNEY	
Toxic nephropathy (rat/NTP 1988)	0.00034 (10)
LIVER	
↑ liver weight (mouse/Kjellstrand et al. 1983b)	0.90 (10)
IMMUNOLOGIC	
↓ thymus weight (mouse/Keil et al. 2009)	0.00048 (100)
REPRODUCTIVE	
↓ ability of sperm to fertilize (rat/DuTeaux et al. 2004)	0.016 (1000)
Multiple effects (rat/Kumar et al. 2000a, 2001b)	0.016 (1000)
Hyperzoospermia (human/Chia et al. 1996)[c]	0.024 (30)
DEVELOPMENTAL	
↓ PFC, ↑ DTH (rat/Peden-Adams et al. 2006)*	0.00037 (1000)
Heart malformations (rat/Johnson et al. 2003)	0.00051 (10)

*cRfD for this study based on applied dose (PBPK modeling not done)

Dose-Response: Cancer

Inhalation

- Kidney cancer inhalation unit risk- human epidemiologic data
- Adjustment to inhalation unit risk to account for risks of lymphomas and liver cancer as well
  - Use human epidemiologic data on TCE for relative risks to derive potency for lymphomas and liver cancer relative to potency for kidney cancer
  - Adjustment factor ≈ 4, so risk for all three sites combined = risk for kidney alone × 4

Oral

- Oral slope factor from route-to route extrapolation using all the same cancer outcomes and combined